Comparative Effectiveness of Dexamethasone versus Prednisone in Children Hospitalized with Asthma

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Objectives To study the comparative effectiveness of dexamethasone vs prednisone/prednisolone in children hospitalized with asthma exacerbation not requiring intensive care.

Study design This multicenter retrospective cohort study, using the Pediatric Health Information System, included children aged 4-17 years who were hospitalized with a principal diagnosis of asthma between January 1, 2007 and December 31, 2012. Children with chronic complex condition and/or initial intensive care unit (ICU) management were excluded. Propensity score matching was used to detect differences in length of stay (LOS), re-admissions, ICU transfer, and cost between groups.

Results 40 257 hospitalizations met inclusion criteria; 1166 (2.9%) received only dexamethasone. In the matched cohort (N = 1284 representing 34 hospitals), the LOS was significantly shorter in the dexamethasone group compared with the prednisone/prednisolone group. The proportion of subjects with a LOS of 3 days or more was 6.7% in the dexamethasone group and 12% in the prednisone/prednisolone group ($P = .002$). Differences in all-cause readmission at 7- and 30 days were not statistically significant. The dexamethasone group had lower costs of index admission ($2621 vs $2838; $P < .001$) and total episode of care (including readmissions) ($2624 vs $2856; $P < .001$) compared with the prednisone/prednisolone group. There were no clinical significant differences in ICU transfer or readmissions between groups.

Conclusions Dexamethasone may be considered an alternative to prednisone/prednisolone for children hospitalized with asthma exacerbation not requiring admission to intensive care. *(J Pediatr 2015;167:639-44)*.

Asthma affects more than 7 million children under 18 years of age.[1,2] Asthma exacerbations are the second most common reason for pediatric hospital admissions.[3] In 2009, there were over 137 000 pediatric hospital admissions for asthma in the US, with direct costs of approximately $500 million dollars.[4] Evidence-based guidelines published by the National Institutes of Health recommend systemic corticosteroid therapy in conjunction with beta-agonist therapy to treat acute asthma exacerbations.[5] Prednisone and its metabolite prednisolone, in the dose 1-2 mg per kg per day for 3-5 days, have traditionally been used to manage acute asthma exacerbations. Recently, dexamethasone administered in the emergency department (ED) setting has been found to be equally effective in treating mild to moderate exacerbations of asthma.[6-8]

Prednisone, or prednisolone, typically used as an oral tablet or syrup, is a relatively short-acting corticosteroid with a half-life of 12 to 36 hours, thereby requiring daily or twice daily dosing. Prolonged treatment course, vomiting, and bitter taste may reduce patient adherence to prednisone or prednisolone prescription.[9] Alternatively, dexamethasone is a long-acting corticosteroid with a half-life of 36 to 72 hours, and therefore a single dose or two doses administered over 2 days are considered to be equivalent to a 5-day course of prednisone or prednisolone. Dexamethasone has a greater affinity for the glucocorticoid receptor compared with methylprednisolone, prednisolone, or prednisone, and is 5 times more potent when receptor affinity and pharmacokinetics are considered together.[10] Dexamethasone is also well-absorbed by both oral and intramuscular routes of administration.[11,12] In addition, dexamethasone is generally considered more palatable than prednisone or prednisolone, with less emesis and better adherence.[11] Therefore, dexamethasone may improve medication adherence due to less frequent dosing, a shorter duration of treatment and better taste (when administered orally) compared with prednisone or prednisolone.

ED	Emergency department
HHI	Household income
ICU	Intensive care unit
LOS	Length of stay
PHIS	Pediatric Health Information System

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Randomized trials have compared the use of dexamethasone vs prednisone/prednisolone in the ED setting for mild or moderate exacerbations of asthma.[6-8,13-15] Most studies have compared 1-2 doses of oral dexamethasone or one dose of intramuscular dexamethasone with a traditional 5-day course of oral prednisone for children discharged from the ED. Gordon et al showed that a single intramuscular dose of dexamethasone did not result in meaningful differences in mean total asthma scores at 4-day follow-up for children discharged from the ED with moderate asthma exacerbation.[13] Qureshi et al compared 2 doses of oral dexamethasone with 5 days of oral prednisone and found that 2 doses of oral dexamethasone were equally effective, and were associated with improved adherence and fewer side effects.[6] Altamimi et al reported that a single dose of oral dexamethasone was no worse than a 5-day course of prednisone in mild or moderate asthma exacerbations.[7] Many ED providers now use dexamethasone in clinical practice, perhaps because it may be considered a more patient-centered treatment plan given the shorter course. However, little is known about the use of dexamethasone for acute exacerbation of asthma in children requiring hospitalization.

The objective of this study was to examine the comparative effectiveness of dexamethasone vs prednisone or prednisolone in children hospitalized with asthma exacerbation requiring non-intensive care admission on presentation. The primary outcome of the study was length of stay (LOS). Secondary outcomes included readmissions, cost, and transfer to intensive care unit (ICU) after admission.

Methods

We used data from the Pediatric Health Information System (PHIS) (Children's Hospital Association, Overland Park, Kansas). PHIS database includes clinical and billing data from 42 freestanding, tertiary care children's hospitals and accounts for approximately 20% of all US pediatric hospitalizations. De-identified data are submitted by participating hospitals. An encrypted medical record number permits identification of readmissions and resource utilization at the same hospital. Data quality is ensured through a joint effort between the Children's Hospital Association and participating hospitals as previously described.[16] In accordance with the policies of the Cincinnati Children's Hospital Medical Center Institutional Review Board, this research, using a de-identified data set, was not considered human subjects research.

Children aged 4-17 years were eligible for inclusion if they were hospitalized between January 1, 2007 and December 31, 2012 with an *International Classification of Diseases, 9th Revision, Clinical Modification* coded principal diagnosis of asthma (493.x). We included children 4 years and older in order to focus on patients with an established diagnosis of asthma. To identify a population of otherwise-well patients admitted for nonsevere asthma exacerbations, we excluded children requiring ICU management on presentation, children with an All-Patient Refined Diagnosis-Related Group severity level of moderate or extreme and, using a previously defined classification scheme, children with complex chronic conditions.[17] Hospitalizations with secondary diagnoses other than asthma that require corticosteroids (eg, croup, anaphylactic shock) were also excluded through independent reviews followed by group consensus when discrepancies arose; patients who received inhaled racemic epinephrine were also excluded to remove patients who may be treated for croup. Finally, when children had multiple asthma hospitalizations within a 30-day period, only the first admission was included; subsequent admissions within the 30-day period were considered readmissions (**Figure**; available at www.jpeds.com).

Exposures

Corticosteroid treatment for asthma exacerbation was classified as dexamethasone for children who received dexamethasone only, and as prednisone or prednisolone for children who received either prednisone or prednisolone only. Patients who received a combination of dexamethasone and either prednisone or prednisolone were excluded from the analysis. Both parenteral and enteral formulations of dexamethasone as well as prednisone or prednisolone were included.

Outcomes

The main outcome measure was total LOS for the index hospitalization. LOS is calculated based on admission and discharge calendar days. Additional outcomes included 7- and 30-day readmissions, cost of index hospitalization, as well as the episode of inpatient care, which includes the cost of the index admission and any readmissions, and transfer to ICU after admission. Costs were estimated using hospital-specific cost-to-charge ratios and adjusted for hospital location using the Centers for Medicare and Medicaid price/wage index.

Covariates

Model covariates included patient demographics (age, race, payer, median annual household income [HHI]), diagnostic tests received (chest radiography), treatments received (antibiotics, magnesium, and/or terbutaline use), and potential confounding patient factors (obesity and/or atopy). *International Classification of Diseases, 9th Revision, Clinical Modification* codes were also used to define obesity[18] (278.00-278.02) and atopy (692.9, 691.8, 477.x, and 478) based on review of secondary discharge diagnosis codes for the study cohort. Median annual HHI, based on patients' home zip codes, were categorized into 4 levels: HHI-1: $34 575 or less, HHI-2: $34 576-$46 100, HHI-3: $46 101-$69 150, HHI-4: $69 151 or more. These levels were based on US Federal poverty guidelines for a family of 4. The HHI-1 limit is 1.5 times the poverty level income; HHI-2 is 1.5-2 times that; HHI-3 is 2-3 times, and HHI-4 is greater than 3 times the poverty level.